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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/836,712	04/17/2001	Leonard Buckbinder	PC10851A	7154

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EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	

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DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/836,712	BUCKBINDER ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 1/12/04, is acknowledged.

2. Claims 33-38 are pending and under examination as they read on a polypeptide of SEQ ID NO:2 comprising metalloproteinase domain, disintegrin domain, prodomain, and thrombospodin submotif thereof.

3. The amendment filed 04/17/01 stands objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The "incorporated by reference" to U.S. application serial no. 60/200,040 on page 1 of the specification does not enjoy the status as part of the original disclosure in the application because the amendment is not referred to in the oath.

Applicant submits that he will submit a new oath to refer to the Preliminary Amendment in due course.

4. The oath or declaration stands defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: the oath does not refer to the preliminary amendment filed 04/17/01.

Applicant submits that he will submit a new oath to refer to the Preliminary Amendment in due course.

5. The objection to the drawings submitted on 6/18/03 stands objected to please see the enclosed form PTO-948 for the Draftsperson comments on views not labeled separately for Figures 1 and 3-4. Applicants are required to amend the Brief Description of the Drawings on page 7 to reflect the changes.

Applicant submits that he will submit corrected formal drawings in due course.

6. In view of the amendment filed on 1/12/04, only the following rejections are remained.

7. 35 U.S.C. § 101 reads as follows:
"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

8. Claims 33-38 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the same reasons set forth in the previous Office Action mailed 9/09/03.

Applicant's arguments, filed 1/12/04, have been fully considered, but have not been found convincing.

Applicant submits that the specification clearly describes the function and activities of the claimed ADAMTS-M polypeptide. Specifically, the ADAMTS-M polypeptide is identified in the specification as a member of the ADAMTS family of metalloproteases - it is apparent that the ADAMTS-M polypeptide functions as a metalloprotease. As further described in the specification at page 14, lines 3-6, ADAMTS-M may have one or more specific proteolytic activities (e.g., collagenase, aggrecanase, procollagen protease), as well as anti-angiogenic activities. Applicant submits that the activities of the ADAMTS-M protein, identified in the specification, are supported by the significant degree of sequence similarity in the metalloprotease domain shared by the ADAMTS-SI protein and other known polypeptides of the ADAMTS family, as described on page 14, lines 3-4 of the specification and illustrated in Figure 4. The asserted activities of the ADAMTS-M protein are also supported by the overall domain organization shared by the ADAMTS-SI protein and other members of the ADAMTS family, as depicted in Figure 3. Applicant submits that in light of these characterizations, the asserted activities of the ADAMTS-M protein would be considered credible by those skilled in the art.

However, such assertion is made based on that ADAMTS-M has 28-32% identity to other ADAMTS family members metalloprotease domain. Further Lu et al (Biochem Biophys Res Commun. 1994 Oct 28;204(2):930-936) teach a novel human and mouse IA-2 protein that possesses highly conserved regions similar to the catalytic domains found in members of the protein tyrosine phosphatase (PTP) family. The mouse sequence shares a high degree of homology with its human counterpart (92% identity), especially in the intracellular domain, which shows 99.3% identity between the two species. However, Lu et al show that the mIA2 have not enzyme activity. Lu et al concluded that the mIA2 is a new member of the transmembrane PTP family, but lacks enzymatic activity wherein mIA2 has very narrow substrate specificity or has a still unknown biological function (see abstract in particular). Therefore, assignment to a prior art family of proteins is insufficient to meet the utility requirement unless such assignment would allow the artisan to assign a specific and substantial use to the new member of the protein family.

Applicant submits that the specification has also asserted number of specific utilities of the ADAMTS-M protein, including employing the protein in the treatment of a number of disorders such as arthritis, atherosderosis, aortic aneurysm, congestive heart failure, myocardial infarction, stroke, cerebral ischemia, ocular angiogenesis, among others.

However, the specification has not disclosed a specific disease or disorder of any type wherein the claimed polypeptides are expressed at altered amounts or forms relative to the required

control healthy tissue. Significant further research would be required of the skilled artisan to identify such a disease or disorder. Therefore the asserted utility is not substantial.

Applicant draws the Examiner's attention to Gerritsen et al. (Blood 98: 1654-1661, 2001) (Exhibit 1); Fujikawa et al. (Blood 98: 1662-1666, 2001) (Exhibit 2); and Levy et al. (Nature 413: 488-494, 2001) (Exhibit 3) to support the claimed actvities.

However, Gerritsen et al and Fujikawa et al identify ADAMTS13 only as a protease that can cleave plasma von Willebrand factor (VWF), a catalytic activity that was not disclosed in the specification as originally filed. Further Levy et al demonstrate that patients with a rare familial form of TTP have inherited mutations in ADAMTS13 which is characterized by decreased levels of proteolysis of vWF in patients. However, the asserted utility does not provide disorders that are characterized by accumulation of vWF, wherein administration of ADAMTS-M polypeptide would inhance vWF -cleaving activity.

Furthermore, the ADAMTS13 polypeptide taught by Gerritsen et al, Fujikawa et al and Levy et al has high homology (98.1%) to the claimed ADAMTS-M. It is noted that amino acids 1-23 of claimed ADAMTS-M are missing from the reference sequences. Further, aa 1156-1190 of Gerritsen et al, Fujikawa et al and Levy et al are not part of the ADAMTS-M sequence.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 33-38 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention so that it would operate as intended without undue experimentation for the same reasons set forth in the previous Office Action mailed 9/09/03.

Further, besides the polypeptide or a composition of SEQ ID NO: 2 and metalloproteinase (aa 98-311 of SEQ ID NO:2), disintegrin domain (aa 324-394 of SEQ ID NO: 2), prodomain (aa 1-97 of SEQ ID NO:2), and thrombospondin submotif (aa 410-473 and 1099-1156 of SEQ ID NO:2) the specification fails to provide any guidance as to how to make any polypeptide "comprising" the metalloproteinase domain, the disintegrin domain, the prodomain domain or amino acids 410-473 and 1099-1156 of SEQ ID NO: 2 in claim 34-37 or a pharmaceutical composition comprising the polypeptides in claim 38.

Applicant's arguments, filed 1/12/04, have been fully considered, but have not been found convincing.

Applicant submits that those skilled in the art would be able to make and use the polypeptides as claimed in claims 33-38.

However, the term "comprising" in claims 34-37 is open ended and extend the polypeptide to include additional amino acids on either or both sides of the C-terminal and N-terminal of the metalloproteinase domain, the disintegrin domain, the prodomain domain or amino acids 410-473 and 1099-1156. A person of skill in the art would not know what particular sequence lengths identify essential sequences. There is insufficient guidance to direct a person of skill in the art to select particular sequences or sequence lengths. Without detailed direction as to which amino acid sequences are essential to the function of the polypeptide, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of amino acid sequences encompassed by the instant claims would share the function of the polypeptide of SEQ ID NO:2, other than the amino acid of SEQ ID NO:2.

Regarding the pharmaceutical composition, Applicant did not address the issue.

11. Claims 33-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action mailed 9/09/03.

Applicant is in possession of the polypeptide or a composition of SEQ ID NO: 2 and metalloproteinase (aa 98-311 of SEQ ID NO:2), disintegrin domain (aa 324-394 of SEQ ID NO: 2), prodomain (aa 1-97 of SEQ ID NO:2), and thrombospondin submotif (aa 410-473 and 1099-1156 of SEQ ID NO:2).

Applicant is not in possession of any polypeptide "comprising" the metalloproteinase domain, the disintegrin domain, the prodomain domain or amino acids 410-473 and 1099-1156 of SEQ ID NO: 2 in claim 34-37 or a pharmaceutical composition comprising the polypeptides in claim 38.

Applicant's arguments, filed 1/12/04, have been fully considered, but have not been found convincing.

Applicant submits that those skilled in the art would be able to make and use the polypeptides as claimed in claims 33-38.

Applicant submits that new claims 33-38 are directed to the polypeptide of SEQ ID NO: 2 and the specific domains thereof which, as the Examiner has acknowledged are adequately described in the specification.

Contrary to Applicant assertions the Examiner did not acknowledged that any polypeptide comprising the specific domains of SEQ ID NO: 2 with undefined sequence length.

12. No claim is allowed.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maher Haddad, Ph.D.
Patent Examiner
March 19, 2004

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